REMARKS

The specification and claims 13, 14, and 15 have been amended to correct an error of a typographical nature. In particular, the R^{12} designation of Phe for PTR 3205 is a duplication of the R^{13} substituent and should not be present. This is clearly shown in Example 2, wherein the detailed synthesis of PTR 3205 is disclosed. By following this synthesis, the structure of PTR-3205 is correctly disclosed as:

Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Cys*-Phe(N3)-X

This sequence is known in the art to have the correct formula shown above (see Falb et al., "*In situ* generation of Fmoc-amino acid chlorides for extremely difficult couplings to sterically hindered secondary amines in solid phase peptides synthesis," Proceedings of the 16th American Peptide Symposium, June 26-July 1, 1999, a copy of which is enclosed).

Thus no new matter is introduced by these changes, so that their entry at this time is appropriate. The marked versions of the amendments to the specification are in Appendix A. The proposed amendments are shown on Appendix B, while a complete set of pending claims is presented in Appendix C.

No fee is believed to be due for this submission. Should any fees be required, please charge them to Winston & Strawn deposit account no. 501-814.

A new power of attorney is enclosed. Please direct cell further communication to Customer No. 28765.

Respectfully submitted,

Date 8/20/01

Allan A. Fanucci 30,256
Allan A. Fanucci (Reg. No.)

WINSTON & STRAWN
200 Park Avenue
New York, New York, 10166

(212) 294-3311

Enclosure

APPENDIX A

MARKED VERSION OF AMENDED PARAGRAHS IN THE SPECIFICATION

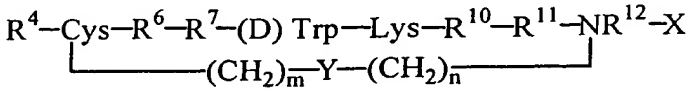
On page 7, please replace old Table 1 with the following new Table:

Table 3. The most preferred analogs.

PTR	Sequence
3171	Phe*-Phe-Phe-(D)Trp-(D)Lys-Phe(C2)-X
3113	Phe(C1)-Phe-Phe-(D)Trp-Lys-Phe(N2)-X
3123	Phe(C1)-Phe-Phe-(D)Trp-(D)Lys-Phe(N2)-X
3209	Phe(N2)-Tyr-(D)2Nal-Lys-Val-Gly(C2)-Thr-X
3183	Phe(N2)-Tyr-(D)Trp-Lys-Val-Gly(C2)-2Nal-X
3185	Phe(N2)-Tyr-(D)Trp-Lys-Val-Val-Gly(C2)-X
3201	Phe(N2)-Tyr-(D)Trp-Lys-Ser-2Nal-Gly(C2)-X
3203	Phe(N2)-Phe-(D)Trp-Lys-Thr-2Nal-Gly(C2)-X
3173	GABA*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X
3197	Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X
3205	Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Cys*-[Phe-]Phe(N3)-X
3207	(D)Phe-Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X
3229	Galactose-Dab*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X

On page 22, please replace the paragraph beginning with "Another preferred embodiment" with the following paragraph:

Another preferred embodiment has the general formula:



Formula No. 14

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^4 is (D)- or (L)-Phe or Tyr;

R^6 is (D)- or (L)-Phe or Tyr;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

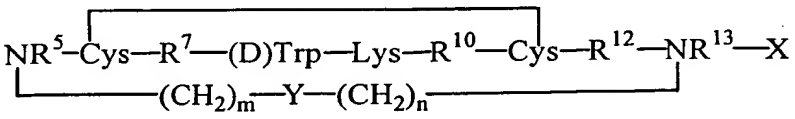
R^{11} is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^{12} is Gly, Val, [or](D)- or (L)-Phe or is absent; and

Y^2 is thioether, thioester or disulfide.

Also on page 23, please replace the paragraph starting with "Another more perferred embodiment" with the following paragraph:

Another more preferred embodiment has the general formula:



Formula No. 15

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^5 is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{12} is Gly, Val, [or](D)- or (L)-Phe or is absent;

R^{13} is (D)- or (L)-Phe or (D)- or (L)-Ala; and

Y^2 is amide, thioether, thioester or disulfide.

Page 26, please replace old Table 3 with the following new Table 3:

Table 3. The most preferred analogs.

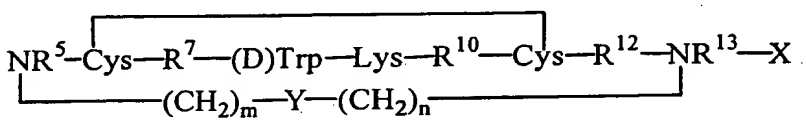
PTR	Sequence
3171	Phe*-Phe-Phe-(D)Trp-(D)Lys-Phe(C2)-X
3113	Phe(C1)-Phe-Phe-(D)Trp-Lys-Phe(N2)-X
3123	Phe(C1)-Phe-Phe-(D)Trp-(D)Lys-Phe(N2)-X
3209	Phe(N2)-Tyr-(D)2Nal-Lys-Val-Gly(C2)-Thr-X
3183	Phe(N2)-Tyr-(D)Trp-Lys-Val-Gly(C2)-2Nal-X
3185	Phe(N2)-Tyr-(D)Trp-Lys-Val-Val-Gly(C2)-X
3201	Phe(N2)-Tyr-(D)Trp-Lys-Ser-2Nal-Gly(C2)-X

3203	Phe(N2)-Phe-(D)Trp-Lys-Thr-2Nal-Gly(C2)-X
3173	GABA*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X
3197	Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X
3205	Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Cys*-[Phe-]Phe(N3)-X
3207	(D)Phe-Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X
3229	Galactose-Dab*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X

APPENDIX B

MARKED VERSION OF THE CLAIMS THE CLAIMS

13. The backbone cyclized somatostatin analog of claim 1 having the general formula 15:



Formula No. 15

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^5 is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{12} is Gly, Val, [or] (D)- or (L)-Phe, or is absent;

R^{13} is (D)- or (L)-Phe or (D)- or (L)-Ala; and

Y^2 is amide, thioether, thioester or disulfide.

14. The backbone cyclized somatostatin analog of claim 13 wherein:

R^5 is Phe;

R^7 is Phe;

R^{10} is Thr;

R^{12} is Gly, Val, [or] (D)- or (L)-Phe, or is absent;

R^{13} is Phe; and

Y^2 is amide.

15. The backbone cyclized somatostatin analog of claim 1 having the formula:

Phe(N2)-Tyr-(D)2Nal-Lys-Val-Gly(C2)-Thr-X;
Phe(N2)-Tyr-(D)Trp-Lys-Val-Gly(C2)-2Nal-X;
Phe(N2)-Tyr-(D)Trp-Lys-Val-Val-Gly(C2)-X;
Phe(N2)-Tyr-(D)Trp-Lys-Ser-2Nal-Gly(C2)-X;
Phe(N2)-Phe-(D)Trp-Lys-Thr-2Nal-Gly(C2)-X;
GABA*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X;
Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X;
Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Cys*-[Phe-]Phe(N3)-X;
(D)Phe-Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X; or
Galactose-Dab*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X;

wherein X designates a terminal carboxy acid, amide, or alcohol group; the asterisk denotes that the bridging group is connected between the N^{α}-ω-functionalized derivative of an amino acid and the N-terminus of the peptide or the side chain of the Cys residue.

APPENDIX C

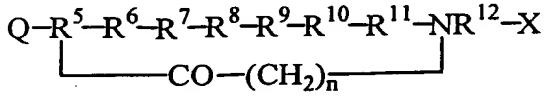
CLAIMS UPON ENTRY OF PRELIMINARY AMENDMENT

THE CLAIMS

What is claimed is:

1. A backbone cyclized somatostatin analog that incorporates at least one building unit, said building unit containing one nitrogen atom of the peptide backbone connected to a bridging group comprising an amide, thioether, thioester, or disulfide, wherein the at least one building unit is connected via the bridging group to form a cyclic structure with a moiety selected from the group consisting of a second building unit, the side chain of an amino acid residue of the sequence or the N-terminal amino acid residue.

2. The backbone cyclized somatostatin analog of claim 1 having the general formula 7:



Formula No. 7

wherein n is 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

Q is hydrogen or a mono- or di- saccharide

R^5 is gamma amino butyric acid, diamino butyric acid, Gly, β-Ala, 5-amino pentanoic acid or amino hexanoic acid;

R^6 is (D)- or (L)-Phe or Tyr;

R^7 is (D)- or (L)-Trp, (D)- or (L)-Phe, (D)- or (L)-1Nal, (D)- or (L)-2Nal, or Tyr;

R^8 is (D)- or (L)-Trp;

R^9 is (D)- or (L)-Lys;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{11} is (D)- or (L)-Phe, (D)- or (L)-Ala, Nle, or Cys; and

R^{12} is Gly, Val, Leu, (D)- or (L)-Phe, 1Nal, or 2Nal.

3. The backbone cyclized somatostatin analog of claim 2 wherein:

Q is hydrogen;

R^5 is GABA;

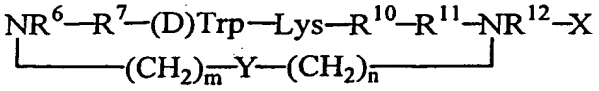
R^6 is Phe;

R^7 is Trp;

R^8 is (D)-Trp;
R^9 is Lys;
R^{10} is Thr;
R^{11} is Phe;
R^{12} is Gly;
n is 3; and
X is an amide.

4. The backbone cyclized somatostatin analog of claim 2 wherein:
Q is galactose;
R^5 is Dab;
R^6 is Phe;
R^7 is (L)-Trp;
R^8 is (D)-Trp;
R^9 is Lys;
R^{10} is Thr;
R^{11} is Phe;
R^{12} is Gly;
n is 3; and
X is an amide.

5. The backbone cyclized somatostatin analog of claim 1 having the general formula 8:



Formula No. 8

wherein: m and n are 1 to 5
X designates a terminal carboxy acid, amide or alcohol group;
R^6 is(D)- or (L)-Phe, or (D)- or (L)-Ala;
R^7 is Tyr, (D)- or (L)- Ala, or (D)- or (L)- Phe;
R^{10} is Thr, Val, Ser, or Cys;
R^{11} is Val, (D)- or (L)-1Nal, (D)- or (L)-2Nal, or (D) or (L)-Phe;
R^{12} is Gly, (D)- or (L)-Ala, or (D) or (L)-Phe; and
Y^2 is amide, thioether, thioester or disulfide.

6. The backbone cyclized somatostatin analog of claim 5 wherein:

R^6 is (D)- or (L)-Phe;

R^7 is Tyr or Phe;

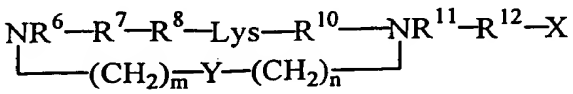
R^{10} is Thr, Val or Ser;

R^{11} is Val, 1Nal, or 2Nal;

R^{12} is Gly; and

Y is amide.

7. The backbone cyclized somatostatin analog of claim 1 having the general formula 9:



Formula No. 9

wherein: m and n are 1 to 5

X designates a terminal carboxy acid, amide or alcohol group;

R^6 is(D)- or (L)-Phe, or (D)- or (L)-Ala;

R^7 is Tyr or (D)- or (L)- Phe;

R^8 is (D)- or (L)- Trp, (D)- or (L)- 1Nal, or (D)- or (L)- 2Nal;

R^{10} is Thr, Val, Ser, or Cys;

R^{11} is Gly or (D) or (L)-Phe;

R^{12} is Thr, GABA, (D)- or (L)- 1Nal, (D)- or (L)- 2Nal, or (D) or (L)-Phe; and

Y is amide, thioether, thioester or disulfide.

8. The backbone cyclized somatostatin analog of claim 7 wherein:

R^6 is (D)- or (L)- Phe;

R^7 is Tyr;

R^8 is (D)Trp, (D)1Nal, or (D)2Nal;

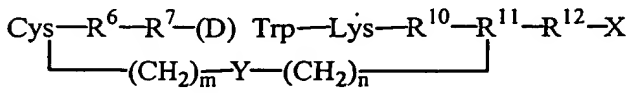
R^{10} is Val;

R^{11} is Gly;

R^{12} is Thr, 1Nal, or 2Nal; and

Y is amide.

9. The backbone cyclized somatostatin analog of claim 1 having the general formula 13:



Formula No. 13

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^6 is (D)- or (L)-Phe or Tyr;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{11} is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^{12} is Gly, Val, or (D)- or (L)-Phe; and

Y^2 is thioether, thioester or disulfide.

10. The backbone cyclized somatostatin analog of claim 9 wherein:

R^6 is Phe;

R^7 is Trp;

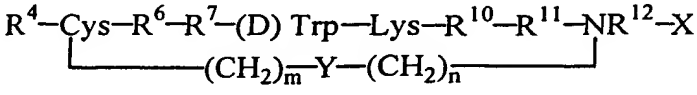
R^{10} is Thr;

R^{11} is Phe;

R^{12} is Gly; and

Y^2 is disulfide.

11. The backbone cyclized somatostatin analog of claim 1 having the general formula 14:



Formula No. 14

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^4 is (D)- or (L)-Phe or Tyr;

R^6 is (D)- or (L)-Phe or Tyr;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{11} is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^{12} is Gly, Val, or (D)- or (L)-Phe; and

Y^2 is thioether, thioester or disulfide.

12. The backbone cyclized somatostatin analog of claim 11 wherein:

R^4 is (D)Phe;

R^6 is Phe;

R^7 is Trp;

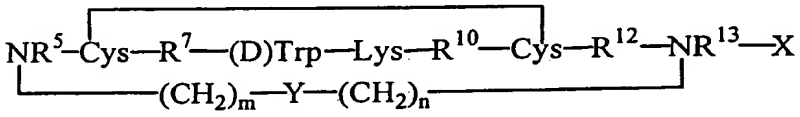
R^{10} is Thr;

R^{11} is Phe;

R^{12} is Gly; and

Y^2 is disulfide.

13. The backbone cyclized somatostatin analog of claim 1 having the general formula 15:



Formula No. 15

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R^5 is (D)- or (L)-Phe or (D)- or (L)-Ala;

R^7 is (D)- or (L)-Trp,(D)- or (L)-Phe, (D)- or (L)- 1Nal or (D)- or (L)- 2Nal, or Tyr;

R^{10} is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{12} is Gly, Val, (D)- or (L)-Phe, or is absent;

R^{13} is (D)- or (L)-Phe or (D)- or (L)-Ala; and

Y^2 is amide, thioether, thioester or disulfide.

14. The backbone cyclized somatostatin analog of claim 13 wherein:

R^5 is Phe;

R^7 is Phe;

R^{10} is Thr;
R^{12} is Gly, Val, (D)- or (L)-Phe, or is absent
R^{13} is Phe; and
Y^2 is amide.

15. The backbone cyclized somatostatin analog of claim 1 having the formula:

Phe(N2)-Tyr-(D)2Nal-Lys-Val-Gly(C2)-Thr-X;
Phe(N2)-Tyr-(D)Trp-Lys-Val-Gly(C2)-2Nal-X;
Phe(N2)-Tyr-(D)Trp-Lys-Val-Val-Gly(C2)-X;
Phe(N2)-Tyr-(D)Trp-Lys-Ser-2Nal-Gly(C2)-X;
Phe(N2)-Phe-(D)Trp-Lys-Thr-2Nal-Gly(C2)-X;
GABA*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X;
Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X;
Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Cys*-Phe(N3)-X
(D)Phe-Cys*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(S2)-X; or
Galactose-Dab*-Phe-Trp-(D)Trp-Lys-Thr-Phe-Gly(C3)-X;

wherein X designates a terminal carboxy acid, amide, or alcohol group; the asterisk denotes that the bridging group is connected between the N^{α}-ω-functionalized derivative of an amino acid and the N-terminus of the peptide or the side chain of the Cys residue.

16. A pharmaceutical composition comprising a backbone cyclized somatostatin analog according to claim 1 and a pharmaceutically acceptable carrier.

17. The composition according to claim 16 wherein the backbone cyclic analog is selective for one somatostatin receptor subtypes.

18. The composition according to claim 16 wherein the backbone cyclic analog is selective for two somatostatin receptor subtypes.

19. A method for treating disorders selected from the group consisting of atherosclerosis, autoimmune diseases, cancers, diabetic-associated complications, endocrine disorders, inflammation, gastrointestinal disorders, pancreatitis, post-surgical pain, and restenosis comprising administering to a mammal in need thereof a pharmaceutical

composition comprising a therapeutically effective amount of a backbone cyclized somatostatin analog according to claim 1.

20. The method according to claim 19 wherein the backbone cyclic analog is selective for one somatostatin receptor subtype.

21. The method according to claim 19 wherein the backbone cyclic analog is selective for two somatostatin receptor subtypes.

22. A method for diagnosing cancer comprising administration of a backbone cyclized somatostatin analog of claim 1.

23. The method according to claim 22 wherein the backbone cyclic analog is used for imaging the existence of metastases.

24. The method according to claim 22 wherein the backbone cyclic analog is labeled with a detectable probe.